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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,682	06/03/2005	Jacques F. Banchereau	BHCS:1028	8543

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EXAMINER	
EWOLDT, GERALD R	

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1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,682	BANCHEREAU ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/3/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I filed 12/08/09 is acknowledged.

2. Claims 44-50 are under examination.

3. The Title is objected to because it does not adequately describe the claimed invention. Applicant is advised that an Title commensurate in scope with the invention of the instant claims is required. In particular the Title must disclose that which is novel to the claimed invention. i.e., a rapid method of generating antigen loaded dendritic cells from monocytes. See MPEP 608.01(b).

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 44-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the claims are vague and indefinite in the recitation of "TNFα" and "pre-processed antigenic material". Regarding "TNFα", the specification defines TNFα as, "any TNF or TNF-like protein which functions as an activator in the methods of this invention". By this definition it is unclear then if Applicant is attempting to define other cytokines such as IL-4 as TNFα, given that IL-4 has the same effect on monocytes in the claimed method. Regarding the "pre-processed antigenic material" of the claims, the term is undefined in the specification. It is unclear how "pre-processed antigenic material" differs from other antigenic material or antigens in general. Accordingly, the metes and bounds of the claims cannot be determined.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear,

> concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 44-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Under *Vas-Cath, Inc. v. Mahurkar* , 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention, and that the invention, in that context, is whatever is now claimed.

There is insufficient written description to show that Applicant was in possession of the tumor necrosis factor alpha (TNFα) of the claims.

At page 17 the specification defines TNFα as, "any TNF or TNF-like protein which functions as an activator in the methods of this invention". A review of the specification shows that even the TNFα employed in the Examples, e.g., page 21, is undefined as to its particular source, i.e., species or whether or not it is actually TNFα or a TNF-like protein. Clearly then no species of the thousands of TNFα's are actually described. No common TNFα structure is defined and neither is a common function. While it could be assumed that the common function might be the ability to induce the differentiation of monocytes into dendritic cells (DCs), the specification merely discloses that TNFα's, "function as an activator in the methods of this invention". Regarding the "TNF-like proteins" of the claimed method, none are defined nor disclosed. Clearly, neither specific structure and function, nor an adequate number of representative species of TNFα, are disclosed in the instant specification. One of skill in the art would therefore conclude that the specification fails to adequately describe TNFα. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

8. Claims 44-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in

the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

Regarding biological methods which rely on previously undescribed and generally unpredictable mechanisms, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)." The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

The instant claims encompass a method for generating DCs from monocytes employing GM-CSF and TNFα. This method has been tried in the prior art and did not result in mature DCs. See Pickl et al. (1996) wherein the authors compared the resulting products of monocytes matured in GM-CSF and IL-4 to the products of monocytes matured in GM-CSF and TNFα. As stated in the Abstract, "Only GM-CSF plus IL-4 cultured cells [monocytes] were found to be potent stimulators in allogeneic and autologous MLR…", i.e., only the GM-CSF plus IL-4 cultured cells were mature DCs. At page 3853 and Figure 5 the reference further teaches that the GM-CSF and TNFα cultured monocytes appeared to

be proliferating, which would not be a characteristic of mature DCs. Figure 9 shows that GM-CSF and TNFα cultured monocytes were only minimally better stimulators of primary T cell responses than were freshly isolated monocytes. It appears then that culture of monocytes in GM-CSF and TNFα results in only partially differentiated DCs and not the mature DCs of the claims.

As set forth in *Rasmusson v. SmithKline Beecham Corp.*, 75 USPQ2d 1297, 1302 (CAFC 2005), enablement cannot be established unless one skilled in the art "would accept without question" an Applicant's statements regarding an invention, particularly in the absence of evidence regarding the effect of a claimed invention. Specifically:

> "As we have explained, we have required a greater measure of proof, and for good reason. If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the "inventor" would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis."

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of sufficient guidance in the specification, and the unpredictability of the art, it would take undue trials and errors to practice the claimed invention.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

10. Claims 44-46 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by U.S. Patent No. 6,479,286.

The '286 patent teaches a method of producing antigen loaded mature DCs comprising the step of maturing monocytes in GM-CSF and TNFα (see particularly Claim 3). Note that the monocytes can be transfected with a gene encoding an antigen of interest thus, producing "the presence of a pre-processed antigenic material" (see particularly column 15).

The reference clearly anticipates the claimed invention.

11. Claims 44-47, 49, and 50 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Romani et al. (1994).

Romani et al. teaches a method of producing antigen loaded mature DCs comprising the step of maturing cord blood mononuclear cells in GM-CSF and TNFα (see particularly page 85). Note that as the DCs matured they would have inherently loaded themselves with antigen. As cord blood comprises T cells as well as monocytes Claim 49 is included in the rejection. As any cell culture would inherently include some cell fractions and dying cell bodies Claim 50 is included in the rejection. As the cell culture medium comprised heat treated FCS, which inherently comprises some antigenic material, (see particularly page 84) Claim 47 is included in the rejection.

The reference clearly anticipates the claimed invention.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on (571) 272-0841.

14. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

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